MEYER et al.

Application No.: 10/006,882

Page 2

1 2

PATENT

LISTING OF CLAIMS:

- 1. (Original) A method for continuous production of Hepatitis A virus,
- 2 comprising the steps of providing a serum free cell culture of VERO cells bound to a
- 3 microcarrier, the method comprising infecting said serum free cell culture of VERO cells with
- 4 HAV, incubating said serum free cell culture of VERO cells infected with HAV to propagate
- 5 said HAV, whereby HAV is continuously released into the cell culture medium; and harvesting
- 6 said HAV released into the cell culture medium.
- 1 2. (Original) The method according to claim 1, wherein said cells are grown 2 at a temperature of about 37°C.
 - 3. (Original) The method according to claim 1, wherein said temperature is reduced to about 34°C prior to infection.
 - 4. (Original) The method of claim 1, wherein the microcarrier is selected from the group of spherical or porous microcarriers.
- 5. (Original) The method according to claim 4, wherein the microcarriers comprise dextran, gelatine, collagen, plastic, or cellulose.
 - 6. (Original) The method according to claim 1, wherein the cells are infected with a seed virus of HAV strain HM175/7.
- 7. (Original) The method according to claim 1, wherein the cells are infected with HAV at a multiplicity of infection between about 0.01 and about 5.0.
- 8. (Original) The method according to claim 1, wherein the cell culture is subcultured from a working cell bank and passaged by use of a microbial protease or a trypsin-like enzyme of a microbial orgin.
- 9. (Original) The method according to claim 8, wherein said microbial
- 2 protease is the trypsin-like enzyme of Streptomyces griseus Pronase.

MEYER et al.

Application No.: 10/006,882

Page 3

2

PATENT

- (Original) The method according to claim 1, wherein HAV is 10. 1 2 continuously produced for at least 60 days.
- (Original) The method according to claim 1, wherein said serum free cell 1 11. culture of VERO cells is a serum and protein free cell culture of VERO cells. 2
- (Original) A method of isolating complete Hepatitis A virus particles, the 12. 1 method of comprising the steps of providing a serum free cell culture of VERO cells bound to a 2 microcarrier, infecting said cell culture with HAV, incubating said cell culture infected with 3 HAV to propagate said HAV, whereby HAV is continuously released into the cell culture 4 medium; harvesting said HAV released into the cell culture medium; and isolating complete 5
- HAV particles from said HAV harvest of the cell culture supernatant. 6
 - (Original) The method according to claim 12, wherein said cells are 13. grown at a temperature of about 37°C prior to infection.
- (Original) The method according to claim 12, wherein the cell culture 14. 1 2 temperature is reduced to about 34°C after infection.
- (Original) The method of claim 12, wherein the microcarrier is selected 15. 1 from the group of smooth microcarriers or porous microcarriers. 2
- (Original) The method according to claim 15, wherein the microcarriers 16. 1 comprise dextran, collagen, plastic, polyethylene or cellulose. 2
- (Original) The method according to claim 12, wherein the cells are 1 17. 2 infected with a seed virus of HAV strain HM175/7.
- (Original) The method according to claim 12, wherein the cell culture is 1 18. subcultured from a working cell bank and passaged by use of a microbial protease or a trypsin-2 3 like enzyme of a microbial protease.
- (Original) The method according to claim 18, wherein said microbial protease is the 19. 1 2 purified trypsin-like enzyme f Streptomyces griseus pronase.

PATENT

MEYER pet al. Application No.: 10/006,882 Page 4

(Original) The method according to claim 12, wherein HAV is 20. continuously produced for at least 60 days.

(Original) The method according to claim 12, wherein the complete HAV particles are isolated by isopycnic centrifugation.

22-23. (Cancelled).

1 2